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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,798	10/18/2000	Xavier Paliard	PP01521.101	3092

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Anne S Dollard
Chiron Corporation
P O Box 8097
Intellectual Property R338
Emeryville, CA 94662-8097

EXAMINER
LI, QIAN J

ART UNIT	PAPER NUMBER
1632	9

DATE MAILED: 06/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/673,798	Applicant(s) PALIARD, XAVIER	
	Examiner Janice Li	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

DETAILED ACTION

The amendment filed on March 28, 2002 has been entered as Paper # 8. The examiner assigned to examine the application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Q. Janice Li, at Group Art Unit 1632.

Unless otherwise indicated, previous rejections that rendered moot in view of the amendment or new grounds of rejections to pending claims will not be reiterated.

Election/Restrictions

In light of Applicants' request, two Groups have been rejoined and examined, which are not thought to place an undue search burden upon the Examiner.

Claims 1-29 are pending and under current examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 9, 11, and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for enhancing an antibody-based immune response to HIV gag by intramuscular or intradermal injection of nucleic acids encoding HIV gag and B lymphocyte chemokine, does not reasonably provide

enablement for enhancing a cytotoxic T lymphocyte response to any antigen and by any means of administration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention (see *In re Wands*, 858 F. 2d 731, 737, 8 USPQ 2d 1400, 1404, 1988). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided.

The claims are drawn to a method of enhancing an immune response to a DNA immunogen in a mammal, wherein the chemokine is B lymphocyte chemokine (BLC). The specification exemplifies in example 2 how BLC increases the titer of anti-p55gag antibodies via muscle injection. However, the specification fails to teach whether BLC would increase antibody responses to other antigens, particularly antigens that do not usually cause an antibody response, whether it could enhance a cellular immune response, and it fails to teach whether any route of administration could enhance such response.

The specification cited *Gunn et al* (Nature 1998 Feb 19;391:799) to define BLC. *Gunn et al* teach that BLC strongly attracts B lymphoctes while promoting migration of only small number of T cells and macrophages, and is the first chemokine to be

identified that is selective towards B cells. The specification fails to show otherwise, thus, the claims do not appear to be enabled commensurate to its scope.

In view of the state of the art in the routes of genetic vaccination, *McCluskie et al* (Mol Med 1999 May;5:287-300) teach "ROUTES OF ADMINISTRATION OF PLASMID DNA VACCINES INFLUENCES THE STRENGTH AND NATURE OF IMMUNE RESPONSES IN MICE AND NON-HUMAN PRIMATES. HOWEVER, THE RESULTS IN MICE WERE NOT ALWAYS PREDICTIVE OF THOSE IN MONKEYS AND THIS IS LIKELY TRUE FOR HUMANS AS WELL. OPTIMAL DOSE AND IMMUNIZATION SCHEDULE WILL MOST LIKELY VARY BETWEEN SPECIES. IT IS NOT CLEAR WHETHER RESULTS IN NON-HUMAN PRIMATES WILL BE PREDICTIVE OF RESULTS IN HUMANS, THUS ADDITIONAL STUDIES ARE REQUIRED." (See abstract) *Nakano et al* (J Virol 1997;71:7101-09) teach that immune reactivity with plasmid DNA encoding HCV-E2 antigenic domains is linked to the injection mode, "DIFFERENT ROUTES OF INJECTION OF HCV E2 PLASMID CAN RESULT IN QUANTITATIVELY AND QUALITATIVELY DIFFERENT HUMORAL IMMUNE RESPONSES" (see abstract).

In view of such, the invention does not appear to be enabled absence of clarification of the contradictory evidence found in the references.

Therefore, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims are vague and indefinite because claim 25 is drawn to a polynucleotide that encodes an HIV polypeptide, but depends on a claim (23) that encodes a hepatitis C virus non-structural polypeptide, which do not embrace an HIV polypeptide.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 8, 10-13, 16, 17, 21, 27, and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by *Chandrashekar et al* (US 6,383,774).

These claims are drawn to an immunogenic composition comprising a DNA immunogen, a chemokine or a polynucleotide encoding a chemokine, preferably MIP-1a, and a pharmaceutically acceptable carrier. The claims are further drawn to a method comprising administering to a mammal a chemokine and a DNA immunogen,

wherein the chemokine may be administered at the same time with the administration of a DNA immunogen, wherein the mammal is human, wherein the immune response is an antibody or cytotoxic T lymphocyte response.

Chandrashekar et al teach an immunogenic composition comprising a nucleic acid encoding a parasitic immunogen and a method for administering such to a mammal including human to protect animals from disease caused by parasitic nematodes (abstract). They go on to teach that the composition can include an adjuvant capable of enhancing the immune response and suitable adjuvants such as chemokines, particularly MIP-1α (1st paragraph column 26), in the case of a nucleic acid vaccine, a DNA encoding the chemokine could be used. They also teach antibody response (column 22, lines 40-66, for example) and the pharmaceutically acceptable adjuvants (2nd & 3rd paragraphs, column 26). Thus, *Chandrashekar et al* anticipate the instant claims.

Claims 1, 2, 5, 8, 10-13, 16, 17, 21, 25, and 27-29 are rejected under 35 U.S.C. 102(e) as being anticipated by *Hurwitz et al* (US 5,846,546).

These claims are drawn to an immunogenic composition comprising a DNA immunogen and a chemokine or a polynucleotide encoding a chemokine, preferably MIP-1α, and a method comprising administering to a mammal a chemokine and a DNA immunogen, wherein the immunogen comprises a polynucleotide encoding a viral immunogen, preferably a HIV polypeptide, wherein the chemokine may be administered at the same time with the administration of a DNA immunogen, wherein the mammal is

human, wherein the immune response is an antibody or cytotoxic T lymphocyte response.

Hurwitz et al teach an immunogenic composition comprising a viral vector encoding HIV envelop protein coding region (abstract), and further or additionally comprising a polynucleotide encoding a chemokine such as MIP1α (2nd paragraph column 29). The composition is suitable for vaccination in mammals including humans (2nd paragraph column 1), and could induce both antibody and cytotoxic T lymphocyte response (column 2, lines 46-55). A pharmaceutical carrier is taught throughout the teachings in columns 28-31. Thus, *Hurwitz et al* anticipate the instant claims.

Claims 1-8, 10-13, 16, 17, 21, 23-29 are rejected under 35 U.S.C. 102(e) as being anticipated by *Selby et al* (US 6,355,247).

These claims are drawn to an immunogenic composition comprising a DNA immunogen and a chemokine or a polynucleotide encoding a chemokine, preferably MIP-1α, and a method comprising administering to a mammal a chemokine and a DNA immunogen, wherein the immunogen comprises a polynucleotide encoding a tumor or viral immunogen, such as HIV gag, and HCV NSs, wherein the chemokine may be administered at the same time with the administration of a DNA immunogen, wherein the mammal is human, wherein the immune response is an antibody or cytotoxic T lymphocyte response.

Selby et al teach an immunogenic composition comprising a nucleic acid vector encoding a viral or tumor antigen and immunomodulatory molecule (column 9, lines

40-45), for example chemokine such as MIP1α (2nd paragraph column 29). The exemplified viral antigens include HCV, NS3-NS5 (example 1), and HIV envelop proteins, and equally applicable to other immunogenic proteins such as gag and pol (paragraph bridging columns 7-8). The recited tumor antigens including MAGE and Mart1 (column 8, lines 20-32). The composition is suitable for vaccination in vertebrates including human (column 1), and could induce both antibody and cytotoxic T lymphocyte response (column 2, lines 46-55). A pharmaceutical carrier is taught in lines 27-39 in column 13. Thus, *Selby et al* anticipate the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 10-21, and 23-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Hurwitz et al* (US 5,846,546) and *Selby et al* (US 6,355,247) as applied to claims 1-8, 10-13, 16, 17, 21, 23-29 above, and further in view of *DeVico et al* (US 6,214,540).

Claims are further drawn to the scheduling of administration regarding the two components of the immunogenic composition, particularly the timing of administration of the DNA immunogen and the chemokine in separation.

Hurwitz et al and Selby et al teach administration of two components together, Hurwitz also teach that chemokine could be administered further or in addition to the immunogen. Although they do not spell out the scheduling of separate administration, it is considered as routine optimization within the knowledge of those skilled in the art.

DeVico et al teach using chemokines for HIV therapy including using chemokine protein and nucleic acid encoding chemokines (section 4.4.1). And how one could personalize the treatment.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Hurwitz et al, Selby et al*, and DeVico et al by administering the immunogen and chemokine together or separate with a reasonable expectation of success because even chmokine alone could achieve a therapeutic effect. The ordinary skilled artisan would have been motivated to modify the method for enhanced immune response against virus and tumor. Thus, the claimed invention as a whole was clearly *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 8, 10-13, 16, 17, 21, and 23-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 5-14, and 16-19 of U.S. Patent No. 6,355,247. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims encompass the claims of cited patent.

Although the conflicting claims are not identical, they are not patentably distinct from each other because Claims 11-13, 16, 17, and 23-29 of the present application and the claims 1, 3, 5-14, and 16-19 of the cited patent are each drawn to a method to generating and enhancing an immune response to a DNA immunogen, particularly, HIV and HCV.

The processes of the present application and the cited patent differ one from the other in that the cited patent does not particularly recite the chemokines, and do not claim the composition. However, they are fully taught in the specification. Accordingly, the claimed processes in the copending and the present application are obvious variants.

Therefore, the inventions as claimed are co-extensive.

Conclusion

No claim is allowed. Claims 9 and 22 appear to be free of cited prior art of record, however, they are subject to other rejections.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
June 14, 2002

JAMES KETTER
PRIMARY EXAMINER